

In the Claims

1-55. (Canceled)

56. (Previously presented) A composition of matter comprising a human or simian IL-7 conformer, wherein said conformer comprises the following three disulfide bridges: Cys: 1-4 (Cys2-Cys92); 2-5 (Cys34- Cys129) and 3-6 (Cys47-Cys141), wherein the total amount by weight of said IL-7 conformer in said composition of matter is at least 98% by weight and wherein said composition of matter is substantially free of IL-7 molecular variants or product related impurities.

57. (Currently amended) The composition of matter according to claim 56, wherein said IL-7 conformer is a recombinant human IL-7 conformer that is not immunogenic in humans.

58. (Previously presented) The composition of matter according to claim 57, wherein said IL-7 conformer comprises the amino acid sequence of SEQ ID NO: 2 or 4.

59. (Withdrawn-Currently amended) The composition of matter according to claim 56, wherein said IL-7 conformer is a recombinant simian IL-7 conformer that is not immunogenic in non-human primates.

60. (Withdrawn) The composition of matter according to claim 59, wherein said IL-7 conformer comprises the amino acid sequence of SEQ ID NO: 12.

61. (Previously presented) The composition of matter according to claim 56, wherein said IL-7 conformer is not glycosylated.

62. (Previously presented) The composition of matter according to claim 56, wherein said IL-7 conformer is glycosylated.

63. (Previously presented) The composition of matter according to claim 56, wherein said IL-7 conformer is associated to the hepatocyte growth factor as a heterodimer.

64. (Previously presented) The composition of matter according to claim 56, wherein said IL-7 conformer is functionally attached to a Fc portion of an IgG heavy chain through a peptide hinge region, said IgG being a human IgG1 or IgG4.

65. (Previously presented) The composition of matter according to claim 56, wherein said IL-7 conformer is functionally associated to a Human Serum Albumin (HSA) or a portion of HSA as a fusion protein.

66. (Currently amended) The composition of matter according to claim 56, wherein said composition of matter ~~being~~is substantially free of another IL-7 conformer.

67. (Previously presented) The composition of matter according to claim 56, wherein the total amount by weight of IL-7 in said composition of matter is at least 99.5% by weight.

68. (Previously presented) A pharmaceutical composition comprising an effective amount of a human or simian IL-7 conformer, wherein said conformer comprises the following three disulfide bridges: Cys: 1-4 (Cys2-Cys92); 2-5 (Cys34- Cys129) and 3-6 (Cys47-Cys141), wherein at least 98% of the total amount by weight of IL-7 consists of said conformer and wherein said composition is substantially free of IL-7 molecular variants or product related impurities, and one or more pharmaceutically acceptable carriers.

69. (Previously presented) The pharmaceutical composition according to claim 68, wherein the pharmaceutically acceptable carrier is selected from sucrose, trehalose and an amino acid.

70. (Previously presented) The pharmaceutical composition according to claim 69, wherein the pharmaceutically acceptable carrier is contained in an appropriate buffer to form an isotonic solution.

71. (Previously presented) The pharmaceutical composition according to claim 70, wherein said appropriate buffer has a pH range of between 5 to 7.5.

72. (Previously presented) The pharmaceutical composition according to claim 71, wherein said appropriate buffer is an organic salt selected from a sodium citrate buffer or an ammonium acetate buffer.

73. (Previously presented) The pharmaceutical composition according to claim 68, wherein said composition is a lyophilized form.

74. (Previously presented) The pharmaceutical composition according to claim 68, wherein said composition further comprises a protein or a surfactant.

75. (Previously presented) The pharmaceutical composition according to claim 68, further comprising an immuno-stimulating agent selected from a hematopoietic cell growth factor, a cytokine, an antigen and an adjuvant, or a combination thereof, for combined, separate or sequential use.

76. (Previously presented) The pharmaceutical composition according to claim 75, wherein said hematopoietic cell growth factor is selected from the Stem Cell Factor (SCF), particularly the soluble form of the SCF, G-CSF, GM-CSF, Flt-3 ligand, IL-15 and IL-2.

77. (Previously presented) The pharmaceutical composition according to claim 75, wherein the cytokine is selected from γ interferon, IL-2, IL-12, RANTES, B7-1, MIP-2 and MIP-1 α .

78. (Previously presented) The pharmaceutical composition according to claim 75, wherein said antigen is selected from a synthetic or natural peptide, a recombinant protein, a killed, inactivated or attenuated pathogen product, a lipid, a portion thereof and a combination thereof.

79. (Previously presented) The pharmaceutical composition according to claim 78, wherein said antigen is selected from antigens derived from HIV, Varicella Zoster virus, Influenza virus, Epstein Barr virus, type I or 2 Herpes Simplex virus, human cytomegalovirus, Dengue virus, Hepatitis A, B, C or E virus, Respiratory Syncytium virus, human papilloma virus, mycobacterium tuberculosis, Toxoplasma and Chlamydia.

80. (Previously presented) The pharmaceutical composition according to claim 75, wherein said adjuvant is selected from any substance, mixture, solute or composition facilitating or increasing the immunogenicity of an antigen and able to induce a Th1-type immune response.

81-84. (Canceled)

85. (Previously presented) The pharmaceutical composition according to claim 68, wherein the effective amount of said IL-7 conformer is between about 3 to 300 µg/kg/day or between 10 to 100 µg/kg/day.

86. (Withdrawn) A nucleic acid molecule encoding an IL-7 polypeptide, wherein said nucleic acid molecule comprises an altered Shine-Dalgarno-like sequence.

87. (Withdrawn) A nucleic acid molecule comprising a sequence selected from SEQ ID Nos: 1, 3, 12, 16, 18, 20 or 22.

88. (Withdrawn) A vector comprising a nucleic acid according to claim 86.

89. (Withdrawn) A recombinant host cell comprising a nucleic acid according to claim 87 or a vector containing said nucleic acid.

90. (Withdrawn) The recombinant host cell according to claim 89, wherein said recombinant host cell is a human cell or a bacterial cell.

91. (Withdrawn) The recombinant host cell according to claim 90, which is *Escherichia coli* or *Bacillus brevis*.

92. (Withdrawn) The recombinant host cell according to claim 90, which is a Chinese Hamster Ovary (CHO) cell line, HEK-293 cell line or a human stromal or epithelial cell line.

93. (Withdrawn) An antibody specifically immunoreactive with an IL-7 conformer as defined in claim 56.

94. (Withdrawn) A method of producing an IL-7 drug substance as defined in claim 56, the method comprising:

- a) providing a sample comprising IL-7 polypeptides,
- b) purifying an IL-7 conformer which comprises the following three disulfide bridges: Cys: 1-4 (Cys2- Cys92); 2-5 (Cys34- Cys129) and 3-6 (Cys47- Cys141) to produce an IL-7 drug substance, and
- c) optionally, measuring or quantifying, in the drug substance, said particular IL-7 conformer.

95. (Withdrawn) The method according to claim 94, wherein said sample is obtained from recombinant prokaryotic or eukaryotic host cells producing IL-7 polypeptides.

96. (Withdrawn) The method according to claim 95, wherein said sample is or derives from a culture of prokaryotic host cells encoding an IL-7 polypeptide and further wherein the method further comprises, prior to step b):

- i) treating said sample to cause a complete denaturation of said IL-7 polypeptides,
- ii) optionally purifying the denatured polypeptide obtained in step i) and
- iii) refolding the polypeptides.

97. (Withdrawn) The method according to claim 96, wherein step i) comprises the dissolution of inclusion bodies in a denaturant buffer.

98. (Withdrawn) The method according to claim 96, wherein step ii) is performed by hydrophobic chromatography, ion-exchange or inverse phase chromatography.

99. (Withdrawn) The method according to claim 97, wherein said hydrophobic chromatography is implemented using HIC butyl.

100. (Withdrawn-Currently amended) The method according to claim 96, wherein step ii) is carried out at a pH comprised between 6 and 9, preferably between 7 and ~~8.5~~ 8.5 inclusive.

101. (Withdrawn) The method according to claim 96, wherein said purification step b) comprises the performance of an affinity chromatography.

102. (Withdrawn) The method according to claim 101, wherein said affinity chromatography is performed on a column of sulfated polysaccharides.

103. (Withdrawn) The method according to claim 102, wherein the sulfated polysaccharide is dextran sulfate or heparin.

104. (Withdrawn-Currently amended) The method according to claim 94, wherein the IL-7 conformer is characterized in the drug substance by Mass spectrometry, infra-red spectroscopy, NMR, by determining ~~circular-diehroism~~ dichroism, by measuring the affinity toward a specific monoclonal antibody raised against said IL-7 conformer, or heparin affinity chromatography, and measured or quantified by ELISA, bioassay or the affinity of said IL-7 conformer for IL-7 receptor and any method of protein quantification if applied to the isolated conformer.

105. (Withdrawn) A method of controlling an IL-7-containing preparation, comprising determining the presence and/or relative quantity, in said preparation, of an IL-7 conformer as defined in claim 56.

106. (Withdrawn) A method of producing an IL-7 drug substance or pharmaceutical composition, said method comprising (i) culturing a recombinant host cell encoding an IL-7 polypeptide, (ii) isolating said recombinant polypeptide to produce an IL-7 drug substance and (iii) optionally, conditioning said IL-7 drug substance to produce a pharmaceutical composition suitable for therapeutic or vaccine use, said method further comprising a step of identifying, characterizing or measuring, in said drug substance or pharmaceutical composition, the quantity and/or quality of an IL-7 conformer as defined in claim 56 and, more preferably, a step of selecting the drug substance or pharmaceutical composition which comprises, as the active ingredient, more than about 98% of said IL-7 conformer.

107. (Withdrawn) The method according to claim 95, wherein IL-7 expression by the recombinant host cells is inducible, regulated or transient, so that the cell culture and IL-7 expression phases can be dissociated.

108. (Withdrawn) The method according to claim 106, wherein the quantity and/or quality of said IL-7 conformer is determined by mass spectrometry-related methods, with or without tryptic digest, circular dichroism, NMR, specific monoclonal antibody analysis for disulfide bridges and/or conformation characterization.

109. (Withdrawn) A method for inducing a prolonged lymphopoiesis stimulation or for amplifying an immune response in a subject, comprising administering to a subject in need thereof an effective amount of an IL-7 drug substance obtained by a method according to claim 94.

110. (Withdrawn) A method for preventing or treating a disease associated with an immunodeficiency, comprising administering to a subject in need thereof an effective amount of an IL-7 drug substance obtained by a method according to claim 94.

111. (Previously presented) The composition of matter according to claim 56, wherein said IL-7 conformer is a human IL-7 conformer.

112. (Withdrawn) The composition of matter according to claim 56, wherein said IL-7 conformer is a simian IL-7 conformer.

113. (Previously presented) The pharmaceutical composition according to claim 68, wherein said IL-7 conformer is a human IL-7 conformer.

114. (Withdrawn) The pharmaceutical composition according to claim 68, wherein said IL-7 conformer is a simian IL-7 conformer.

115 (new). A composition of matter comprising a human or simian IL-7 conformer, wherein said conformer comprises the following three disulfide bridges: Cys: 1-4 (Cys2- Cys92); 2-5 (Cys34- Cys129) and 3-6 (Cys47- Cys141), wherein the total amount by weight of said IL-7 conformer in said composition of matter is at least 98% by weight, wherein said composition of matter is substantially free of IL-7 molecular variants or product related impurities, and wherein said composition of matter is produced by a method comprising (i) culturing a recombinant host cell encoding an IL-7 polypeptide, (ii) isolating and conditioning said recombinant polypeptide to produce an IL-7 composition of matter suitable for therapeutic or vaccine use, said method further

comprising a step of identifying, characterizing or measuring, in said composition of matter, the quantity and/or quality of an IL-7 conformer.

116 (new). The composition according to claim 115, wherein the step of identifying, characterizing or measuring, in said composition of matter, the quantity and/or quality of an IL-7 conformer comprises conducting Mass spectrometry, infra-red spectroscopy, NMR, circular dichroism determination, measuring the affinity toward a specific monoclonal antibody raised against said IL-7 conformer, or heparin affinity chromatography.

117 (new). A composition of matter comprising a human or simian IL-7 conformer, wherein said conformer comprises the following three disulfide bridges: Cys: 1-4 (Cys2- Cys92); 2-5 (Cys34- Cys129) and 3-6 (Cys47- Cys141), wherein the total amount by weight of said IL-7 conformer in said composition of matter is at least 98% by weight, wherein said composition of matter is substantially free of IL-7 molecular variants or product related impurities and wherein the human IL-7 conformer is not immunogenic in humans and the simian IL-7 conformer is not immunogenic in non-human primates.

118 (new). The composition according to claim 117, which is produced by a method comprising (i) culturing a recombinant host cell encoding an IL-7 polypeptide, (ii) isolating and conditioning said recombinant polypeptide to produce an IL-7 composition of matter suitable for therapeutic or vaccine use, said method further comprising a step of identifying, characterizing or measuring, in said composition of matter, the quantity and/or quality of an IL-7 conformer, and a step of assessing immunogenicity of composition.